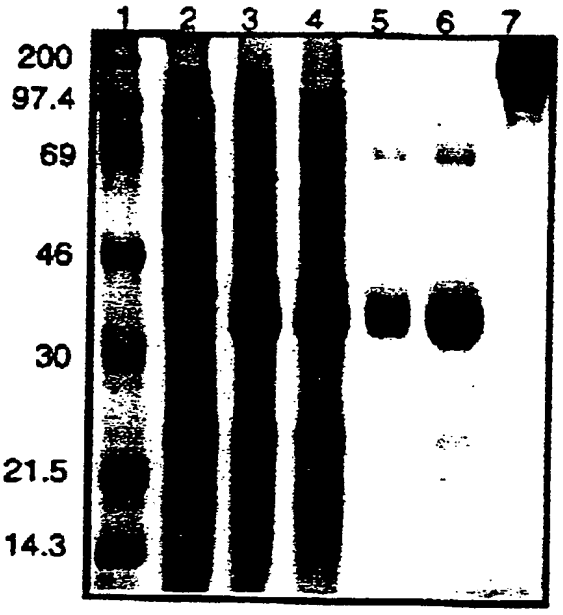

Fig. 1

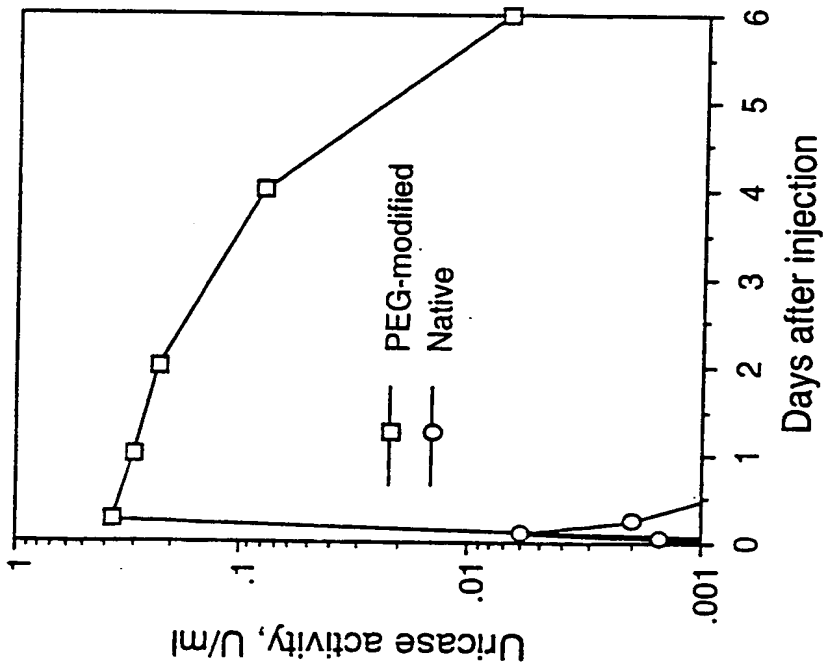
Uricase activity, U/ml
1
.1
.01
.001
0
1
2
3
4
5
6
Days after injection
PEG-modified
Native

Fig. 2

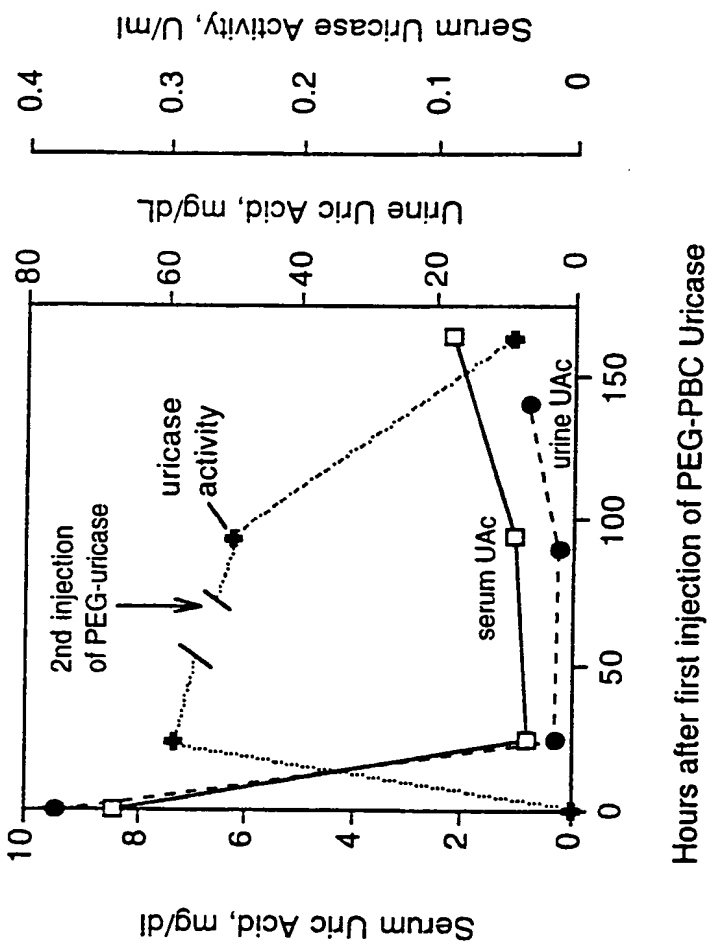
Serum Uricase Activity, U/ml
0.4
0.3
0.2
0.1
0
Urine Uric Acid, mg/dL
80
60
40
20
0
2nd injection of PEG-uricase
uricase activity
serum UAc
urine UAc
10
8
6
4
2
0
0
50
100
150
Serum Uric Acid, mg/dl
Hours after first injection of PEG-PBC Uricase

Fig. 3

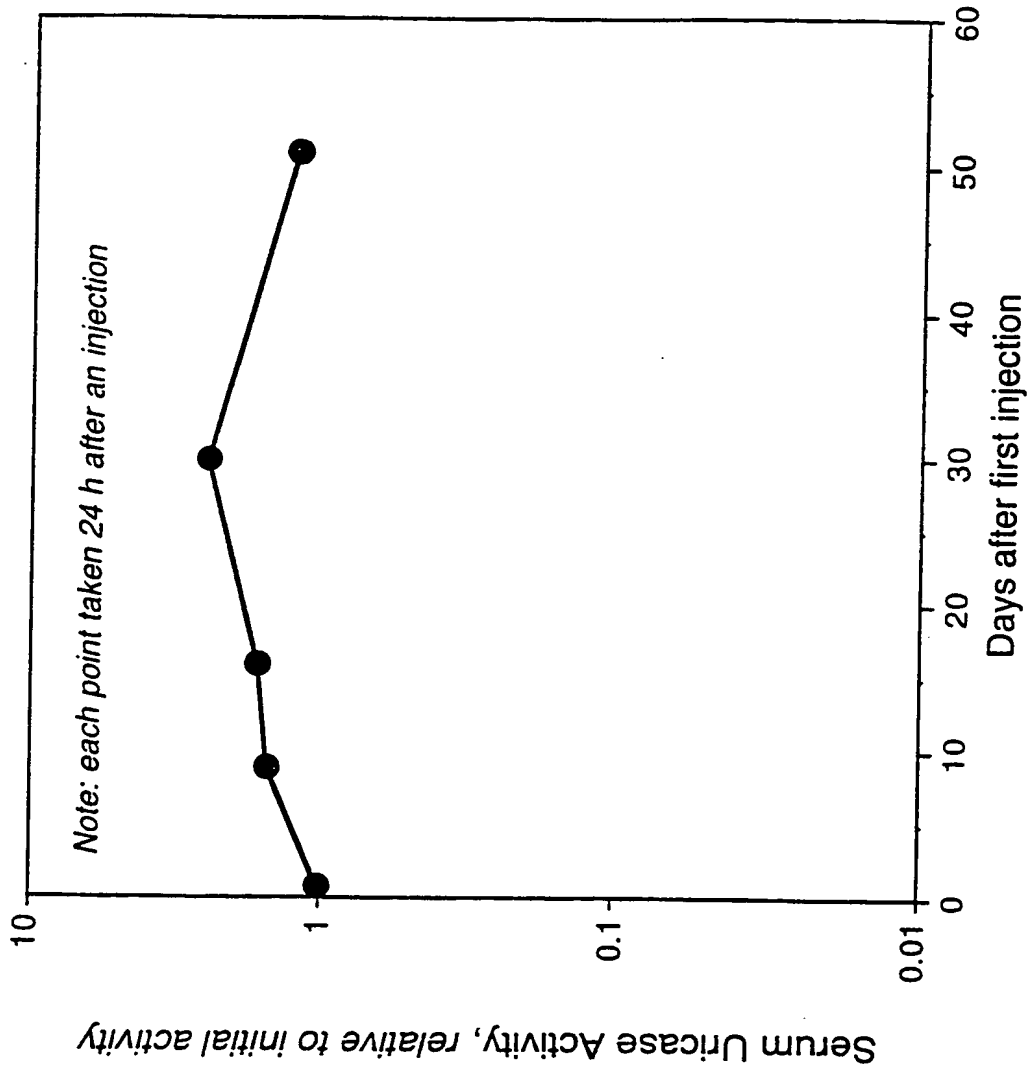
Serum Uricase Activity, relative to initial activity
10
1
0.1
0.01
0
10
20
30
40
50
60
Days after first injection
Note: each point taken 24 h after an injection

Fig. 4

Fig. 5

Deduced Amino Acid Sequences of Pig-Baboon Chimeric Uricase (PBC Uricase)

and Porcine Uricase Containing the Mutations R291K and T301S (PKS Uricase), Compared with the Porcine and Baboon Sequences

Porcine	MAHYRNDYKK NDEVEFVRTG YGKDMIKVLH IQRDGKYHSI	40
PBC	1-225 porcine sequence →	
PKS	1-288 porcine sequence →	
Baboon	MADYHNNYKK NDELEFVRTG YGKDMVKVLH IQRDGKYHSI	40
Porcine	KEVATSVQLT LSSKKDYLHG DNSDVIPTDT IKNTVNVLAK	80
PBC	*porcine sequence* →	
PKS	*porcine sequence* →	
Baboon	KEVATSVQLT LSSKKDYLHG DNSDIIPTDT IKNTVHVLAK	80
Porcine	FKGIKSIETF AVTICEHFLS SFKHVIRAQV YVEEVPWKRF	120
PBC	*porcine sequence* →	
PKS	*porcine sequence* →	
Baboon	FKGIKSIEAF GVNICEYFLS SFNHVIRAQV YVEEIPWKRL	120
Porcine	EKNGVKHVHA FIYTPTGTHF CEVEQIRNGP PVIHSGIKDL	160
PBC	*porcine sequence* →	
PKS	*porcine sequence* →	
Baboon	EKNGVKHVHA FIHTPTGTHF CEVEQLRSGP PVIHSGIKDL	160
Porcine	KVLKTTQSGF EGFIKDQFTT LPEVKDRCFA TQVYCKWRYH	200
PBC	*porcine sequence* →	
PKS	*porcine sequence* →	
Baboon	KVLKTTQSGF EGFIKDQFTT LPEVKDRCFA TQVYCKWRYH	200
Porcine	QGRDVDFEAT WDTVRSIVLQ KFAGPYDKGE YSPSVQKTLY	240
PBC	*porcine sequence* → | ← *baboon sequence*	
PKS	*porcine sequence* →	
Baboon	QCRDVDFEAT WGTIRDLVLE KFAGPYDKGE YSPSVQKTLY	240
Porcine	DIQVLTLGQV PEIEDMEISL PNIHYLNIDM SKMGLINKEE	280
PBC	*baboon sequence* →	
PKS	*porcine sequence* →	
Baboon	DIQVLSLSRV PEIEDMEISL PNIHYFNIDM SKMGLINKEE	280
Porcine	VLLPLDNPYG RITGTVKRKL TSRL	
PBC	*baboon sequence* → *304*	
PKS	*porcine* | ← *baboon 289-304*	
Baboon	VLLPLDNPYG KITGTVKRKL SSRL	

Fig. 6

Comparison of amino acid sequences "stripped-down" version of chimera, known as "PigKS" (also called "Pig-Lys") vs. Pig uricase

"Pig KS" uricase:
Pig cDNA from 1 to 864 (NdeI site) and then Baboon 865 to 915 (end)

Pig uricase:
Pig cDNA from 1 to 915 (end)

[**GCG GAP program**]
Gap Weight: 12 Average Match: 2.912
Length Weight: 4 Average Mismatch: -2.003

Quality: 1601 Length: 319
Ratio: 5.249 Gaps: 0
Percent Similarity: 99.672 Percent Identity: 99.344

Match display thresholds for the alignment(s):
| = IDENTITY
: = 2
. = 1

pigKS.pep x Pig.pep June 25, 1998 17:11 ..

```
pigKS   1 MAHYRNDYKKNDEVEFVRTGYGKDMIKVLHIQRDGKYHSIKEVATSVQLT 50
          ||||||||||||||||||||||||||||||||||||||||||||||||||
Pig     1 MAHYRNDYKKNDEVEFVRTGYGKDMIKVLHIQRDGKYHSIKEVATSVQLT 50

       51 LSSKKDYLHGDNSDVIPTDTIKNTVNVLAKFKGIKSIETFAVTICEHFLS 100
          ||||||||||||||||||||||||||||||||||||||||||||||||||
       51 LSSKKDYLHGDNSDVIPTDTIKNTVNVLAKFKGIKSIETFAVTICEHFLS 100

      101 SFKHVIRAQVYVEEVPWKRFEKNGVKHVHAFIYTPTGTHFCEVEQIRNGP 150
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      101 SFKHVIRAQVYVEEVPWKRFEKNGVKHVHAFIYTPTGTHFCEVEQIRNGP 150

      151 PVIHSGIKDLKVLKTTQSGFEGFIKDQFTTLPEVKDRCFATQVYCKWRYH 200
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      151 PVIHSGIKDLKVLKTTQSGFEGFIKDQFTTLPEVKDRCFATQVYCKWRYH 200

      201 QGRDVDFEATWDTVRSIVLQKFAGPYDKGEYSPSVQKTLYDIQVLTLGQV 250
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      201 QGRDVDFEATWDTVRSIVLQKFAGPYDKGEYSPSVQKTLYDIQVLTLGQV 250

      251 PEIEDMEISLPNIHYLNIDMSKMGLINKEEVLLPLDNPYGKITGTVKRKL 300
          ||||||||||||||||||||||||||||||||||:||||||||||
      251 PEIEDMEISLPNIHYLNIDMSKMGLINKEEVLLPLDNPYGRITGTVKRKL 300

      301 SSRL*  305
          .||||
      301 TSRL*. 305
```

Fig. 7

Comparison of amino acid sequences of the "original" Pig-baboon chimeric uricase ("chimera") with that of the "stripped-down" version of chimera, known as "PigKS" (also called "Pig-Lys")

"Chimera" uricase:
Pig cDNA from 1 to 674 (Apa site) and then Baboon cDNA from 675 to 915 (end)

"Pig KS" uricase:
Pig cDNA from 1 to 864 (NdeI site) and then Baboon 865 to 915 (end)

```
[GCG GAP program]
        Gap Weight:      12      Average Match:  2.912
     Length Weight:       4   Average Mismatch: -2.003

           Quality:    1589             Length:     319
             Ratio:   5.210               Gaps:       0
Percent Similarity: 98.689   Percent Identity: 98.689

      Match display thresholds for the alignment(s):
                  | = IDENTITY
                  : =    2
                  . =    1

chimera.pep x pigKS.pep   June 25, 1998 16:15  ..

chim.   1 MAHYRNDYKKNDEVEFVRTGYGKDMIKVLHIQRDGKYHSIKEVATSVQLT 50
          ||||||||||||||||||||||||||||||||||||||||||||||||||
PigKS   1 MAHYRNDYKKNDEVEFVRTGYGKDMIKVLHIQRDGKYHSIKEVATSVQLT 50

       51 LSSKKDYLHGDNSDVIPTDTIKNTVNVLAKFKGIKSIETFAVTICEHFLS 100
          ||||||||||||||||||||||||||||||||||||||||||||||||||
       51 LSSKKDYLHGDNSDVIPTDTIKNTVNVLAKFKGIKSIETFAVTICEHFLS 100

      101 SFKHVIRAQVYVEEVPWKRFEKNGVKHVHAFIYTPTGTHFCEVEQIRNGP 150
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      101 SFKHVIRAQVYVEEVPWKRFEKNGVKHVHAFIYTPTGTHFCEVEQIRNGP 150

      151 PVIHSGIKDLKVLKTTQSGFEGFIKDQFTTLPEVKDRCFATQVYCKWRYH 200
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      151 PVIHSGIKDLKVLKTTQSGFEGFIKDQFTTLPEVKDRCFATQVYCKWRYH 200

      201 QGRDVDFEATWDTVRSIVLQKFAGPYDKGEYSPSVQKTLYDIQVLSLSRV 250
          ||||||||||||||||||||||||||||||||||||||||||||.| .|
      201 QGRDVDFEATWDTVRSIVLQKFAGPYDKGEYSPSVQKTLYDIQVLTLGQV 250

      251 PEIEDMEISLPNIHYFNIDMSKMGLINKEEVLLPLDNPYGKITGTVKRKL 300
          |||||||||||||| ||||||||||||||||||||||||||||||||||
      251 PEIEDMEISLPNIHYLNIDMSKMGLINKEEVLLPLDNPYGKITGTVKRKL 300

      301 SSRL*. 305
          |||||
      301 SSRL*  305
```

Fig. 8

Comparison of amino acid sequences of the "original" Pig-baboon chimeric uricase ("chimera") with that of Pig uricase

"Chimera" uricase:
Pig cDNA from 1 to 674 (Apa site) and then Baboon cDNA from 675 to 915 (end)

Pig uricase:
Pig cDNA from 1 to 915 (end)

[GCG GAP program]
Gap Weight: 12 Average Match: 2.912
Length Weight: 4 Average Mismatch: -2.003

Quality: 1583 Length: 305
Ratio: 5.190 Gaps: 0
Percent Similarity: 98.361 Percent Identity: 98.033

Match display thresholds for the alignment(s):
| = IDENTITY
: = 2
. = 1

chimera.pep x Pig.pep June 25, 1998 16:54 ..

```
chim    1 MAHYRNDYKKNDEVEFVRTGYGKDMIKVLHIQRDGKYHSIKEVATSVQLT 50
          ||||||||||||||||||||||||||||||||||||||||||||||||||
Pig     1 MAHYRNDYKKNDEVEFVRTGYGKDMIKVLHIQRDGKYHSIKEVATSVQLT 50

       51 LSSKKDYLHGDNSDVIPTDTIKNTVNVLAKFKGIKSIETFAVTICEHFLS 100
          ||||||||||||||||||||||||||||||||||||||||||||||||||
       51 LSSKKDYLHGDNSDVIPTDTIKNTVNVLAKFKGIKSIETFAVTICEHFLS 100

      101 SFKHVIRAQVYVEEVPWKRFEKNGVKHVHAFIYTPTGTHFCEVEQIRNGP 150
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      101 SFKHVIRAQVYVEEVPWKRFEKNGVKHVHAFIYTPTGTHFCEVEQIRNGP 150

      151 PVIHSGIKDLKVLKTTQSGFEGFIKDQFTTLPEVKDRCFATQVYCKWRYH 200
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      151 PVIHSGIKDLKVLKTTQSGFEGFIKDQFTTLPEVKDRCFATQVYCKWRYH 200

      201 QGRDVDFEATWDTVRSIVLQKFAGPYDKGEYSPSVQKTLYDIQVLSLSRV 250
          ||||||||||||||||||||||||||||||||||||||||||||.| .|
      201 QGRDVDFEATWDTVRSIVLQKFAGPYDKGEYSPSVQKTLYDIQVLTLGQV 250

      251 PEIEDMEISLPNIHYFNIDMSKMGLINKEEVLLPLDNPYGKITGTVKRKL 300
          |||||||||||||||| ||||||||||||||||||||:|||||||||
      251 PEIEDMEISLPNIHYLNIDMSKMGLINKEEVLLPLDNPYGRITGTVKRKL 300

      301 SSRL* 305
          .||||
      301 TSRL* 305
```

Fig. 9

Comparison of amino acid sequence of the "original" Pig-baboon chimeric uricase ("chimera") with that of "Baboon D3H" uricase (Baboon except for His replacing Asp at amino acid 3)

Pig uricase:
Pig cDNA from 1 to 915 (end)

"Baboon D3H" uricase:
"Baboon D3H" cDNA from 1 to 915 (end)

[**GCG GAP program**]

Gap Weight:	12	Average Match:	2.912
Length Weight:	4	Average Mismatch:	-2.003
Quality:	1493	Length:	305
Ratio:	4.895	Gaps:	0
Percent Similarity:	94.098	Percent Identity:	90.820

Match display thresholds for the alignment(s):
| = IDENTITY
: = 2
. = 1

Pig.pep x baboon D3H.pep June 25, 1998 17:44 ..

```
Pig     1 MAHYRNDYKKNDEVEFVRTGYGKDMIKVLHIQRDGKYHSIKEVATSVQLT 50
          ||||  |.||||||.|||||||||||:|||||||||||||||||||||||
Bab     1 MAHYHNNYKKNDELEFVRTGYGKDMVKVLHIQRDGKYHSIKEVATSVQLT 50

       51 LSSKKDYLHGDNSDVIPTDTIKNTVNVLAKFKGIKSIETFAVTICEHFLS 100
          ||||||||||||||:||||||||||.|||||||||||| | | |||:|||
       51 LSSKKDYLHGDNSDIIPTDTIKNTVHVLAKFKGIKSIEAFGVNICEYFLS 100

      101 SFKHVIRAQVYVEEVPWKRFEKNGVKHVHAFIYTPTGTHFCEVEQIRNGP 150
          ||  ||||||||||||:|||| ||||||||||||:||||||||||||:|.||
      101 SFNHVIRAQVYVEEIPWKRLEKNGVKHVHAFIHTPTGTHFCEVEQLRSGP 150

      151 PVIHSGIKDLKVLKTTQSGFEGFIKDQFTTLPEVKDRCFATQVYCKWRYH 200
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      151 PVIHSGIKDLKVLKTTQSGFEGFIKDQFTTLPEVKDRCFATQVYCKWRYH 200

      201 QGRDVDFEATWDTVRSIVLQKFAGPYDKGEYSPSVQKTLYDIQVLTLGQV 250
          | |||||||||  |:| :||:||||||||||||||||||||||||.| .|
      201 QCRDVDFEATWGTIRDLVLEKFAGPYDKGEYSPSVQKTLYDIQVLSLSRV 250

      251 PEIEDMEISLPNIHYLNIDMSKMGLINKEEVLLPLDNPYGRITGTVKRKL 300
          |||||||||||||| ||||||||||||||||||||||:||||||||||
      251 PEIEDMEISLPNIHYFNIDMSKMGLINKEEVLLPLDNPYGKITGTVKRKL 300

      301 TSRL* 305
          .||||
      301 SSRL* 305
```

Fig. 10

Comparison of amino acid sequence of the "original" Pig-baboon chimeric uricase ("chimera") with that of "Baboon D3H" uricase (Baboon except for His replacing Asp at amino acid 3)

"Chimera" uricase:
Pig cDNA from 1 to 674 (Apa site) and then Baboon cDNA from 675 to 915 (end)

"Baboon D3H" uricase:
"Baboon D3H" cDNA from 1 to 915 (end)

[GCG GAP program]

Gap Weight:	12	Average Match:	2.912
Length Weight:	4	Average Mismatch:	-2.003
Quality:	1516	Length:	305
Ratio:	4.970	Gaps:	0
Percent Similarity:	95.738	Percent Identity:	92.787

Match display thresholds for the alignment(s):
| = IDENTITY
: = 2
. = 1

chimera.pep x baboon D3H.pep June 25, 1998 17:18 ..

```
chim    1 MAHYRNDYKKNDEVEFVRTGYGKDMIKVLHIQRDGKYHSIKEVATSVQLT 50
          |||| |.|||||.|||||||||||:|||||||||||||||||||||||||
Bab     1 MAHYHNNYKKNDELEFVRTGYGKDMVKVLHIQRDGKYHSIKEVATSVQLT 50

       51 LSSKKDYLHGDNSDVIPTDTIKNTVNVLAKFKGIKSIETFAVTICEHFLS 100
          ||||||||||||||:||||||||||.|||||||||||| | | |||:|||
       51 LSSKKDYLHGDNSDIIPTDTIKNTVHVLAKFKGIKSIEAFGVNICEYFLS 100

      101 SFKHVIRAQVYVEEVPWKRFEKNGVKHVHAFIYTPTGTHFCEVEQIRNGP 150
          || ||||||||||||:|||| ||||||||||||:|||||||||||||:|.||
      101 SFNHVIRAQVYVEEIPWKRLEKNGVKHVHAFIHTPTGTHFCEVEQLRSGP 150

      151 PVIHSGIKDLKVLKTTQSGFEGFIKDQFTTLPEVKDRCFATQVYCKWRYH 200
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      151 PVIHSGIKDLKVLKTTQSGFEGFIKDQFTTLPEVKDRCFATQVYCKWRYH 200

      201 QGRDVDFEATWDTVRSIVLQKFAGPYDKGEYSPSVQKTLYDIQVLSLSRV 250
          | |||||||||| |:| :||:||||||||||||||||||||||||||||
      201 QCRDVDFEATWGTIRDLVLEKFAGPYDKGEYSPSVQKTLYDIQVLSLSRV 250

      251 PEIEDMEISLPNIHYFNIDMSKMGLINKEEVLLPLDNPYGKITGTVKRKL 300
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      251 PEIEDMEISLPNIHYFNIDMSKMGLINKEEVLLPLDNPYGKITGTVKRKL 300

      301 SSRL* 305
          |||||
      301 SSRL* 305
```

Fig. 11-1

Bestfit (GCG software) comparison of coding sequences of the cDNAs of Pig KS uricase ("PKS") vs. pig uricase

"Pig KS" uricase:
Pig cDNA from 1 to 864 (NdeI site) and then Baboon 865 to 915 (end)

Gap Weight:	50	Average Match:	10.000
Length Weight:	3	Average Mismatch:	-9.000
Quality:	9036	Length:	915
Ratio:	9.875	Gaps:	0
Percent Similarity:	99.344	Percent Identity:	99.344

Match display thresholds for the alignment(s):
| = IDENTITY
: = 5
. = 1

pigKS.seq x pig.seq July 25, 1998 10:14 ..

```
PKS     1 ATGGCTCATTACCGTAATGACTACAAAAAGAATGATGAGGTAGAGTTTGT 50
          ||||||||||||||||||||||||||||||||||||||||||||||||||
pig     1 ATGGCTCATTACCGTAATGACTACAAAAAGAATGATGAGGTAGAGTTTGT 50

       51 CCGAACTGGCTATGGGAAGGATATGATAAAAGTTCTCCATATTCAGCGAG 100
          ||||||||||||||||||||||||||||||||||||||||||||||||||
       51 CCGAACTGGCTATGGGAAGGATATGATAAAAGTTCTCCATATTCAGCGAG 100

      101 ATGGAAAATATCACAGCATTAAAGAGGTGGCAACTTCAGTGCAACTGACT 150
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      101 ATGGAAAATATCACAGCATTAAAGAGGTGGCAACTTCAGTGCAACTGACT 150

      151 TTGAGCTCCAAAAAAGATTACCTGCATGGAGACAATTCAGATGTCATCCC 200
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      151 TTGAGCTCCAAAAAAGATTACCTGCATGGAGACAATTCAGATGTCATCCC 200

      201 TACAGACACCATCAAGAACACAGTTAATGTCCTGGCGAAGTTCAAAGGCA 250
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      201 TACAGACACCATCAAGAACACAGTTAATGTCCTGGCGAAGTTCAAAGGCA 250

      251 TCAAAAGCATAGAAACTTTTGCTGTGACTATCTGTGAGCATTTCCTTTCT 300
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      251 TCAAAAGCATAGAAACTTTTGCTGTGACTATCTGTGAGCATTTCCTTTCT 300

      301 TCCTTCAAGCATGTCATCAGAGCTCAAGTCTATGTGGAAGAAGTTCCTTG 350
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      301 TCCTTCAAGCATGTCATCAGAGCTCAAGTCTATGTGGAAGAAGTTCCTTG 350

      351 GAAGCGTTTTGAAAAGAATGGAGTTAAGCATGTCCATGCATTTATTTATA 400
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      351 GAAGCGTTTTGAAAAGAATGGAGTTAAGCATGTCCATGCATTTATTTATA 400
```

Fig. 11-2

```
401 CTCCTACTGGAACGCACTTCTGTGAGGTTGAACAGATAAGGAATGGACCT 450
    |||||||||||||||||||||||||||||||||||||||||||||||||||
401 CTCCTACTGGAACGCACTTCTGTGAGGTTGAACAGATAAGGAATGGACCT 450

451 CCAGTCATTCATTCTGGAATCAAAGACCTAAAAGTCTTGAAAACAACCCA 500
    |||||||||||||||||||||||||||||||||||||||||||||||||||
451 CCAGTCATTCATTCTGGAATCAAAGACCTAAAAGTCTTGAAAACAACCCA 500

501 GTCTGGCTTTGAAGGATTCATCAAGGACCAGTTCACCACCCTCCCTGAGG 550
    |||||||||||||||||||||||||||||||||||||||||||||||||||
501 GTCTGGCTTTGAAGGATTCATCAAGGACCAGTTCACCACCCTCCCTGAGG 550

551 TGAAGGACCGGTGCTTTGCCACCCAAGTGTACTGCAAATGGCGCTACCAC 600
    |||||||||||||||||||||||||||||||||||||||||||||||||||
551 TGAAGGACCGGTGCTTTGCCACCCAAGTGTACTGCAAATGGCGCTACCAC 600

601 CAGGGCAGAGATGTGGACTTTGAGGCCACCTGGGACACTGTTAGGAGCAT 650
    |||||||||||||||||||||||||||||||||||||||||||||||||||
601 CAGGGCAGAGATGTGGACTTTGAGGCCACCTGGGACACTGTTAGGAGCAT 650

651 TGTCCTGCAGAAATTTGCTGGGCCCTATGACAAAGGCGAGTACTCGCCCT 700
    |||||||||||||||||||||||||||||||||||||||||||||||||||
651 TGTCCTGCAGAAATTTGCTGGGCCCTATGACAAAGGCGAGTACTCGCCCT 700

701 CTGTCCAGAAGACACTCTATGACATCCAGGTGCTCACCCTGGGCCAGGTT 750
    |||||||||||||||||||||||||||||||||||||||||||||||||||
701 CTGTCCAGAAGACACTCTATGACATCCAGGTGCTCACCCTGGGCCAGGTT 750

751 CCTGAGATAGAAGATATGGAAATCAGCCTGCCAAATATTCACTACTTAAA 800
    |||||||||||||||||||||||||||||||||||||||||||||||||||
751 CCTGAGATAGAAGATATGGAAATCAGCCTGCCAAATATTCACTACTTAAA 800

801 CATAGACATGTCCAAAATGGGACTGATCAACAAGGAAGAGGTCTTGCTAC 850
    |||||||||||||||||||||||||||||||||||||||||||||||||||
801 CATAGACATGTCCAAAATGGGACTGATCAACAAGGAAGAGGTCTTGCTAC 850

851 CTTTAGACAATCCATATGGAAAAATTACTGGTACAGTCAAGAGGAAGTTG 900
    |||||||||||||||||||  |  ||||||||||||||||||||||  ||
851 CTTTAGACAATCCATATGGCAGGATTACTGGTACAGTCAAGAGGAAGCTG 900

901 TCTTCAAGACTGTGA 915
    |||||||  ||||||
901 ACTTCAAGGCTGTGA 915
```

SUBSTITUTE SHEET (RULE 26)

Fig. 12-1

Bestfit (GCG software) comparison of coding sequences of the cDNAs of Pig KS uricase ("PKS") vs. baboon uricase

"Pig KS" uricase:
Pig cDNA from 1 to 864 (NdeI site) and then Baboon 865 to 915 (end)

Gap Weight:	50	Average Match:	10.000
Length Weight:	3	Average Mismatch:	-9.000
Quality:	7573	Length:	915
Ratio:	8.277	Gaps:	0
Percent Similarity:	90.929	Percent Identity:	90.929

Match display thresholds for the alignment(s):
| = IDENTITY
: = 5
. = 1

pigKS.seq x baboon.seq July 25, 1998 10:21 ..

```
PKS     1 ATGGCTCATTACCGTAATGACTACAAAAAGAATGATGAGGTAGAGTTTGT 50
          ||||| | |||| ||| |||| ||||||||||||||| | |||||||||
bab     1 ATGGCCGACTACCATAACAACTATAAAAAGAATGATGAATTGGAGTTTGT 50

       51 CCGAACTGGCTATGGGAAGGATATGATAAAAGTTCTCCATATTCAGCGAG 100
          |||||||||||||||||||||||| ||||||||||||||||||||||||
       51 CCGAACTGGCTATGGGAAGGATATGGTAAAAGTTCTCCATATTCAGCGAG 100

      101 ATGGAAAATATCACAGCATTAAAGAGGTGGCAACTTCAGTGCAACTGACT 150
          |||||||||||||||||||||||||||||||||||||||||||||| |||
      101 ATGGAAAATATCACAGCATTAAAGAGGTGGCAACTTCAGTGCAACTTACT 150

      151 TTGAGCTCCAAAAAAGATTACCTGCATGGAGACAATTCAGATGTCATCCC 200
          |||| |||||||||||||||||||||||| |||||||| |||||||
      151 CTGAGTTCCAAAAAAGATTACCTGCATGGAGATAATTCAGATATCATCCC 200

      201 TACAGACACCATCAAGAACACAGTTAATGTCCTGGCGAAGTTCAAAGGCA 250
          |||||||||||||||||||||||| ||||| |||| ||||| || || |
      201 TACAGACACCATCAAGAACACAGTTCATGTCTTGGCAAAGTTTAAGGGAA 250

      251 TCAAAAGCATAGAAACTTTTGCTGTGACTATCTGTGAGCATTTCCTTTCT 300
          |||||||||||||| | |||| ||||| ||| ||||||| |||| ||||||
      251 TCAAAAGCATAGAAGCCTTTGGTGTGAATATTTGTGAGTATTTTCTTTCT 300

      301 TCCTTCAAGCATGTCATCAGAGCTCAAGTCTATGTGGAAGAAGTTCCTTG 350
          || || || ||||| ||| |||||||||||||| |||||||| | ||||||
      301 TCTTTTAACCATGTAATCCGAGCTCAAGTCTACGTGGAAGAAATCCCTTG 350

      351 GAAGCGTTTTGAAAAGAATGGAGTTAAGCATGTCCATGCATTTATTTATA 400
          ||||||| |||||||||||||||||||||||||||||||||||||| | |
      351 GAAGCGTCTTGAAAAGAATGGAGTTAAGCATGTCCATGCATTTATTCACA 400
```

Fig. 12-2

```
401 CTCCTACTGGAACGCACTTCTGTGAGGTTGAACAGATAAGGAATGGACCT 450
    |||| |||||||| |||||||||||| |||||||| | || | |||||||
401 CTCCCACTGGAACACACTTCTGTGAAGTTGAACAACTGAGAAGTGGACCC 450

451 CCAGTCATTCATTCTGGAATCAAAGACCTAAAAGTCTTGAAAACAACCCA 500
    || |||||||||||||||||||||||||| || |||||||||||||| ||
451 CCCGTCATTCATTCTGGAATCAAAGACCTCAAGGTCTTGAAAACAACACA 500

501 GTCTGGCTTTGAAGGATTCATCAAGGACCAGTTCACCACCCTCCCTGAGG 550
    ||||||| |||||||| ||||||||||||||||||||||||||||||||
501 GTCTGGATTTGAAGGTTTCATCAAGGACCAGTTCACCACCCTCCCTGAGG 550

551 TGAAGGACCGGTGCTTTGCCACCCAAGTGTACTGCAAATGGCGCTACCAC 600
    |||||||||| |||||||||||||||||||||||| ||||||||||||
551 TGAAGGACCGATGCTTTGCCACCCAAGTGTACTGCAAGTGGCGCTACCAC 600

601 CAGGGCAGAGATGTGGACTTTGAGGCCACCTGGGACACTGTTAGGAGCAT 650
    ||| |||| |||||||||||| ||||| ||||||| ||| || || | |
601 CAGTGCAGGGATGTGGACTTCGAGGCTACCTGGGGCACCATTCGGGACCT 650

651 TGTCCTGCAGAAATTTGCTGGGCCCTATGACAAAGGCGAGTACTCGCCCT 700
    ||||||| ||||||||||||||||||||||||||||||||||||| ||||
651 TGTCCTGGAGAAATTTGCTGGGCCCTATGACAAAGGCGAGTACTCACCCT 700

701 CTGTCCAGAAGACACTCTATGACATCCAGGTGCTCACCCTGGGCCAGGTT 750
    |||| |||||||| |||||||| |||||||||||| ||||| ||| |||
701 CTGTGCAGAAGACCCTCTATGATATCCAGGTGCTCTCCCTGAGCCGAGTT 750

751 CCTGAGATAGAAGATATGGAAATCAGCCTGCCAAATATTCACTACTTAAA 800
    |||||||||||||||||||||||||||||||||||| |||||||||||
751 CCTGAGATAGAAGATATGGAAATCAGCCTGCCAAACATTCACTACTTCAA 800

801 CATAGACATGTCCAAAATGGGACTGATCAACAAGGAAGAGGTCTTGCTAC 850
    |||||||||||||||||||| |||||||||||||||||||||||||| |
801 TATAGACATGTCCAAAATGGGTCTGATCAACAAGGAAGAGGTCTTGCTGC 850

851 CTTTAGACAATCCATATGGAAAAATTACTGGTACAGTCAAGAGGAAGTTG 900
    | ||||||||||||||||||||||||||||||||||||||||||||||
851 CATTAGACAATCCATATGGAAAAATTACTGGTACAGTCAAGAGGAAGTTG 900

901 TCTTCAAGACTGTGA 915
    |||||||||||||||
901 TCTTCAAGACTGTGA 915
```

FORM PCT/RO/134 (JULY 1992)

Fig. 13-1

Bestfit (GCG software) comparison of coding sequences of the cDNAs of "original" pig-baboon chimeric uricase ("PBC") vs. pig uricase

"PBC" uricase:
Pig cDNA from 1 to 674 (Apa site) then Baboon cDNA from 675 to 915 (end). PBC chimeric cDNA can be cut out with NcoI plus BamHI

```
        Gap Weight:     50      Average Match: 10.000
     Length Weight:      3   Average Mismatch: -9.000

           Quality:   8770              Length:    915
             Ratio:  9.585               Gaps:      0
Percent Similarity: 97.814   Percent Identity: 97.814

      Match display thresholds for the alignment(s):
                 | = IDENTITY
                 : =   5
                 . =   1

PBC.seq x pig.seq        July 25, 1998 08:10  ..

PBC     1 ATGGCTCATTACCGTAATGACTACAAAAAGAATGATGAGGTAGAGTTTGT 50
          ||||||||||||||||||||||||||||||||||||||||||||||||||
PIG     1 ATGGCTCATTACCGTAATGACTACAAAAAGAATGATGAGGTAGAGTTTGT 50

       51 CCGAACTGGCTATGGGAAGGATATGATAAAAGTTCTCCATATTCAGCGAG 100
          ||||||||||||||||||||||||||||||||||||||||||||||||||
       51 CCGAACTGGCTATGGGAAGGATATGATAAAAGTTCTCCATATTCAGCGAG 100

      101 ATGGAAAATATCACAGCATTAAAGAGGTGGCAACTTCAGTGCAACTGACT 150
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      101 ATGGAAAATATCACAGCATTAAAGAGGTGGCAACTTCAGTGCAACTGACT 150

      151 TTGAGCTCCAAAAAAGATTACCTGCATGGAGACAATTCAGATGTCATCCC 200
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      151 TTGAGCTCCAAAAAAGATTACCTGCATGGAGACAATTCAGATGTCATCCC 200

      201 TACAGACACCATCAAGAACACAGTTAATGTCCTGGCGAAGTTCAAAGGCA 250
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      201 TACAGACACCATCAAGAACACAGTTAATGTCCTGGCGAAGTTCAAAGGCA 250

      251 TCAAAAGCATAGAAACTTTTGCTGTGACTATCTGTGAGCATTTCCTTTCT 300
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      251 TCAAAAGCATAGAAACTTTTGCTGTGACTATCTGTGAGCATTTCCTTTCT 300

      301 TCCTTCAAGCATGTCATCAGAGCTCAAGTCTATGTGGAAGAAGTTCCTTG 350
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      301 TCCTTCAAGCATGTCATCAGAGCTCAAGTCTATGTGGAAGAAGTTCCTTG 350

      351 GAAGCGTTTTGAAAAGAATGGAGTTAAGCATGTCCATGCATTTATTTATA 400
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      351 GAAGCGTTTTGAAAAGAATGGAGTTAAGCATGTCCATGCATTTATTTATA 400
```

Fig. 13-2

```
401 CTCCTACTGGAACGCACTTCTGTGAGGTTGAACAGATAAGGAATGGACCT 450
    |||||||||||||||||||||||||||||||||||||||||||||||||||
401 CTCCTACTGGAACGCACTTCTGTGAGGTTGAACAGATAAGGAATGGACCT 450

451 CCAGTCATTCATTCTGGAATCAAAGACCTAAAAGTCTTGAAAACAACCCA 500
    |||||||||||||||||||||||||||||||||||||||||||||||||||
451 CCAGTCATTCATTCTGGAATCAAAGACCTAAAAGTCTTGAAAACAACCCA 500

501 GTCTGGCTTTGAAGGATTCATCAAGGACCAGTTCACCACCCTCCCTGAGG 550
    |||||||||||||||||||||||||||||||||||||||||||||||||||
501 GTCTGGCTTTGAAGGATTCATCAAGGACCAGTTCACCACCCTCCCTGAGG 550

551 TGAAGGACCGGTGCTTTGCCACCCAAGTGTACTGCAAATGGCGCTACCAC 600
    |||||||||||||||||||||||||||||||||||||||||||||||||||
551 TGAAGGACCGGTGCTTTGCCACCCAAGTGTACTGCAAATGGCGCTACCAC 600

601 CAGGGCAGAGATGTGGACTTTGAGGCCACCTGGGACACTGTTAGGAGCAT 650
    |||||||||||||||||||||||||||||||||||||||||||||||||||
601 CAGGGCAGAGATGTGGACTTTGAGGCCACCTGGGACACTGTTAGGAGCAT 650

651 TGTCCTGCAGAAATTTGCTGGGCCCTATGACAAAGGCGAGTACTCACCCT 700
    |||||||||||||||||||||||||||||||||||||||||||| ||||
651 TGTCCTGCAGAAATTTGCTGGGCCCTATGACAAAGGCGAGTACTCGCCCT 700

701 CTGTGCAGAAGACCCTCTATGATATCCAGGTGCTCTCCCTGAGCCGAGTT 750
    |||| ||||||||| |||||||| |||||||||||| |||||| ||| |||
701 CTGTCCAGAAGACACTCTATGACATCCAGGTGCTCACCCTGGGCCAGGTT 750

751 CCTGAGATAGAAGATATGGAAATCAGCCTGCCAAACATTCACTACTTCAA 800
    |||||||||||||||||||||||||||||||| |||||||||||| ||
751 CCTGAGATAGAAGATATGGAAATCAGCCTGCCAAATATTCACTACTTAAA 800

801 TATAGACATGTCCAAAATGGGTCTGATCAACAAGGAAGAGGTCTTGCTGC 850
    |||||||||||||||||||| |||||||||||||||||||||||||| |
801 CATAGACATGTCCAAAATGGGACTGATCAACAAGGAAGAGGTCTTGCTAC 850

851 CATTAGACAATCCATATGGAAAAATTACTGGTACAGTCAAGAGGAAGTTG 900
    | |||||||||||||||||| | ||||||||||||||||||||||||||
851 CTTTAGACAATCCATATGGCAGGATTACTGGTACAGTCAAGAGGAAGCTG 900

901 TCTTCAAGACTGTGA 915
    ||||||| ||||||
901 ACTTCAAGGCTGTGA 915
```

Fig. 14-1

Bestfit (GCG software) comparison of coding sequences of the cDNAs of "original" pig-baboon chimeric uricase ("PBC") vs. baboon uricase

"PBC" uricase:
Pig cDNA from 1 to 674 (Apa site) then Baboon cDNA from 675 to 915 (end). PBC chimeric cDNA can be cut out with NcoI plus BamHI

```
          Gap Weight:     50      Average Match: 10.000
       Length Weight:      3   Average Mismatch: -9.000

             Quality:   7839              Length:    915
               Ratio:  8.567               Gaps:      0
 Percent Similarity: 92.459   Percent Identity: 92.459

        Match display thresholds for the alignment(s):
                    | = IDENTITY
                    : =   5
                    . =   1

 PBC.seq x Wubaboon.seq       July 25, 1998 09:36  ..

PBC     1 ATGGCTCATTACCGTAATGACTACAAAAAGAATGATGAGGTAGAGTTTGT 50
          |||||  | ||||  |||  ||||  ||||||||||||||||  | ||||||||
Bab     1 ATGGCCGACTACCATAACAACTATAAAAAGAATGATGAATTGGAGTTTGT 50

       51 CCGAACTGGCTATGGGAAGGATATGATAAAAGTTCTCCATATTCAGCGAG 100
          |||||||||||||||||||||||||| ||||||||||||||||||||||||
       51 CCGAACTGGCTATGGGAAGGATATGGTAAAAGTTCTCCATATTCAGCGAG 100

      101 ATGGAAAATATCACAGCATTAAAGAGGTGGCAACTTCAGTGCAACTGACT 150
          |||||||||||||||||||||||||||||||||||||||||||||||| |||
      101 ATGGAAAATATCACAGCATTAAAGAGGTGGCAACTTCAGTGCAACTTACT 150

      151 TTGAGCTCCAAAAAAGATTACCTGCATGGAGACAATTCAGATGTCATCCC 200
          ||||  |||||||||||||||||||||||||  |||||||||  ||||||||
      151 CTGAGTTCCAAAAAAGATTACCTGCATGGAGATAATTCAGATATCATCCC 200

      201 TACAGACACCATCAAGAACACAGTTAATGTCCTGGCGAAGTTCAAAGGCA 250
          |||||||||||||||||||||||||  |||||  ||||  |||||  ||  || |
      201 TACAGACACCATCAAGAACACAGTTCATGTCTTGGCAAAGTTTAAGGGAA 250

      251 TCAAAAGCATAGAAACTTTTGCTGTGACTATCTGTGAGCATTTCCTTTCT 300
          ||||||||||||||  | ||||  |||||  |||  ||||||  ||||  ||||||
      251 TCAAAAGCATAGAAGCCTTTGGTGTGAATATTTGTGAGTATTTTCTTTCT 300

      301 TCCTTCAAGCATGTCATCAGAGCTCAAGTCTATGTGGAAGAAGTTCCTTG 350
          ||  ||  ||  |||||  |||  ||||||||||||  |||||||||  | |||||
      301 TCTTTTAACCATGTAATCCGAGCTCAAGTCTACGTGGAAGAAATCCCTTG 350

      351 GAAGCGTTTTGAAAAGAATGGAGTTAAGCATGTCCATGCATTTATTTATA 400
          |||||||  ||||||||||||||||||||||||||||||||||||||  |  |
      351 GAAGCGTCTTGAAAAGAATGGAGTTAAGCATGTCCATGCATTTATTCACA 400
```

Fig. 14-2

```
401 CTCCTACTGGAACGCACTTCTGTGAGGTTGAACAGATAAGGAATGGACCT 450
    ||||  |||||||| |||||||||||| ||||||||   | ||  | ||||||
401 CTCCCACTGGAACACACTTCTGTGAAGTTGAACAACTGAGAAGTGGACCC 450

451 CCAGTCATTCATTCTGGAATCAAAGACCTAAAAGTCTTGAAAACAACCCA 500
    ||  |||||||||||||||||||||||||| ||  ||||||||||||||| ||
451 CCCGTCATTCATTCTGGAATCAAAGACCTCAAGGTCTTGAAAACAACACA 500

501 GTCTGGCTTTGAAGGATTCATCAAGGACCAGTTCACCACCCTCCCTGAGG 550
    ||||||  |||||||| ||||||||||||||||||||||||||||||||||
501 GTCTGGATTTGAAGGTTTCATCAAGGACCAGTTCACCACCCTCCCTGAGG 550

551 TGAAGGACCGGTGCTTTGCCACCCAAGTGTACTGCAAATGGCGCTACCAC 600
    ||||||||||  |||||||||||||||||||||||||  ||||||||||||
551 TGAAGGACCGATGCTTTGCCACCCAAGTGTACTGCAAGTGGCGCTACCAC 600

601 CAGGGCAGAGATGTGGACTTTGAGGCCACCTGGGACACTGTTAGGAGCAT 650
    |||  ||||  |||||||||||  |||||  |||||||  |||   ||  ||   | |
601 CAGTGCAGGGATGTGGACTTCGAGGCTACCTGGGGCACCATTCGGGACCT 650

651 TGTCCTGCAGAAATTTGCTGGGCCCTATGACAAAGGCGAGTACTCACCCT 700
    |||||||  |||||||||||||||||||||||||||||||||||||||||||
651 TGTCCTGGAGAAATTTGCTGGGCCCTATGACAAAGGCGAGTACTCACCCT 700

701 CTGTGCAGAAGACCCTCTATGATATCCAGGTGCTCTCCCTGAGCCGAGTT 750
    |||||||||||||||||||||||||||||||||||||||||||||||||||
701 CTGTGCAGAAGACCCTCTATGATATCCAGGTGCTCTCCCTGAGCCGAGTT 750

751 CCTGAGATAGAAGATATGGAAATCAGCCTGCCAAACATTCACTACTTCAA 800
    |||||||||||||||||||||||||||||||||||||||||||||||||||
751 CCTGAGATAGAAGATATGGAAATCAGCCTGCCAAACATTCACTACTTCAA 800

801 TATAGACATGTCCAAAATGGGTCTGATCAACAAGGAAGAGGTCTTGCTGC 850
    |||||||||||||||||||||||||||||||||||||||||||||||||||
801 TATAGACATGTCCAAAATGGGTCTGATCAACAAGGAAGAGGTCTTGCTGC 850

851 CATTAGACAATCCATATGGAAAAATTACTGGTACAGTCAAGAGGAAGTTG 900
    |||||||||||||||||||||||||||||||||||||||||||||||||||
851 CATTAGACAATCCATATGGAAAAATTACTGGTACAGTCAAGAGGAAGTTG 900

901 TCTTCAAGACTGTGA 915
    ||||||||||||||||
901 TCTTCAAGACTGTGA 915
```

FIGURE 14-2 SHEET 2 OF 2